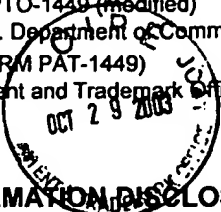


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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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| Atty. Dkt. No. | M# | Client Ref. |
| | 009848-0272496 | C2481/US |
| Applicant: Cevc, et al. | | |
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U.S. PATENT DOCUMENTS

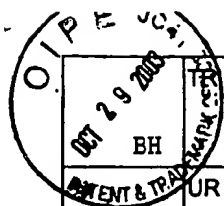
| Examiner's Initials* | Document Number | Date MM/YYYY | Name (Family Name of First Inventor) | Class | Sub Class | Filing Date (if appropriate) |
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FOREIGN PATENT DOCUMENTS

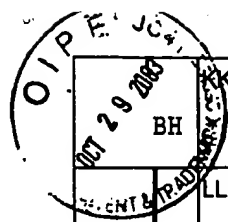
| | Document Number | Date MM/YYYY Y | Country | Inventor Name | English Abstract | | Translation Readily Available | |
|----|-------------------------------|----------------------|---------------|---------------------|---------------------|----|-------------------------------------|----|
| | | | | | Enclosed | No | Enclose | No |
| | BR DE 41 07 152 | 09/1992 | DE | Cevc, G. | | | | |
| | CR DE 44 47 207 | 11/1990 | DE | Cevc, G. | | | | |
| | BR EP 0 475 100 A1 | 08/1991 | EP | Cevc, G. | | | | |
| | CR EP 0 475 100 B1 | 08/1991 | EP | Cevc, G. | | | | |
| BH | FR WO 90/09385 | 08/1990 | WO | Weiner, A.L. | | | | |
| | OR WO 92/03122 | 03/1992 | WO | Cevc, G. | | | | |
| BH | HR WO 92/04009 | 03/1992 | WO | Gregoriadis, G. | | | | |
| | IR WO 98/17233 | 04/1998 | WO | Cevc, G. | | | | |
| BH | JR WO 00/24377 | 05/1998 | WO | Cevc, G. | | | | |
| | KR | | | | | | | |

OTHER (Including in this order Author, Title, Periodical Name, Date, Pertinent Pages, etc.)

| | | | | | | |
|----|----|--|--|--|--|--|
| BH | LR | Almeida, A.J., et al., Nasal delivery of vaccines, J. Drug Targeting, 3:455-467 (1996) | | | | |
| | MR | Bagnasco, M. et al, Absorption and distribution kinetics of the major Parietaria judaica allergen (Par j 1) administered by noninjectable routes in healthy human beings, J.Allergy Clin. Immunol (1997) 100: 122-9 | | | | |
| | NR | Biberoglu, K., et al., Treatment of estrogen-dependent gynecological disorders with the gonadotropin releasing hormone agonist buserelin, Gynecol. Endocrinol. 1991; 5: 109-22 | | | | |
| | OR | Bruins, J., et al., Effect of acute and chronic treatment with desglycinamide-[Arg ⁸]Vasopressin in young male and female volunteers. Peptides, 1995; 16: 179-86 | | | | |
| | PR | Cevc, G., et al., Drug delivery across the skin, Exp. Opin. Invest. Drugs (1997) 6: 1887-1937 | | | | |
| | QR | Cevc, G., Transfersomes, liposomes and other lipid suspensions on the skin: Permeation enhancement, vesicle penetration, and transdermal drug delivery, Critical Reviews in Therapeutic Drug Carrier Systems, 13(3&4):257-388 (1996) | | | | |
| | RR | Cevc, G., et al., Ultraflexible vesicles, transfersomes, have an extremely low permeation resistance and transport therapeutic amounts of insulin across the intact mammalian skin. Biochim. Biophys. Acta 1998; 1368: 201-215 | | | | |
| | SR | Draghia, R., et al., Gene delivery into the central nervous system by nasal instillation in rats. Gene-Ther. 1995; 2: 418-23 | | | | |



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|--|--|-----|---|--|--|--|--|
| | | UR | Drejer, K., et al., Intranasal administration of insulin with phospholipid as absorption enhancer: pharmacokinetics in normal subjects, Diab. Med. 1992, 9:335-340. | | | | |
| | | VR | Flanagan, B., et al., A recombinant human adenovirus expressing the simian immunodeficiency virus Gag antigen can induce long-lived immune responses in mice, J. Gen. Virol. 1997; 78: 991-7 | | | | |
| | | WR | Gizurarson, S., et al., Intranasal administration of insulin to humans. Diabetes Res. Clin. Pract. 1991 May; 12: 71-84 | | | | |
| | | XR | Ghigo, E.; et al., Short-term administration of intranasal or oral Hexarelin, a synthetic hexapeptide, does not desensitize the growth hormone responsiveness in human aging. Eur. J. Endocrinol. 1996; 135: 407-12 | | | | |
| | | YR | Harris, AS, Review: clinical opportunities provided by the nasal administration of peptides. J. Drug Target. 1993; 1: 101-16 | | | | |
| | | ZR | Huneycutt, BS, et al., Distribution of vesicular stomatitis virus proteins in the brains of BALB/c mice following intranasal inoculation: an immunohistochemical analysis, Brain Res. 1994; 635: 81-95 | | | | |
| | | AAR | Hussain A., et al., Does increasing the lipophilicity of peptides enhance their nasal absorption? J. Pharm. Sci. 1991; 80: 11 80-1 | | | | |
| | | BBR | Ichikawa-M, et al., Anti-osteopenic effect of nasal salmon calcitonin in type 1 osteoporotic rats: comparison with subcutaneous dosing, Biol. Pharm. Bull. 1994; 17: 911-13 | | | | |
| | | CCR | Illum, L., The nasal delivery of peptides and proteins. Trends Biotechnol. 1991; 9: 284-9 | | | | |
| | | DDR | Illum, L.; et al., Intranasal insulin. Clinical pharmacokinetics. Clin. Pharmacokinet. 1992 Jul; 23: 30-41 | | | | |
| | | EER | Invitti, C., et al., Effect of chronic treatment with octreotide nasal powder on serum levels of growth hormone, insulin-like growth factor I, insulin-like growth factor binding proteins 1 and 3 in acromegalic patients, J. Endocrinol. Invest. 1996; 19: 548-55 | | | | |
| | | FFR | Kida, S., et al., CSF drains directly from the subarachnoid space into nasal lymphatics in the rat. Anatomy, histology and immunological significance. Neuropathol. Appl. Neurobiol. 1993; 19: 480-448 | | | | |
| | | GGR | Laursen, T., et al., Bioavailability and bioactivity of three different doses of nasal growth hormone (GH) administered to GH-deficient patients: comparison with intravenous and subcutaneous administration, Eur. J. Endocrinol. 1996; 135: 309-15 | | | | |
| | | HHR | Machida, M., et al., Absorption of recombinant human granulocyte colony-stimulating factor (rhG-CSF) from rat nasal mucosa, Pharm. Res. 1993; 10(9): 1372-7. | | | | |
| | | IIR | Maejima, K.; et al., Comparison of the effects of various fine particles on IgE antibody production in mice inhaling Japanese cedar pollen allergens. J. Toxicol. Environ. Health. 1997; 52: 231 -48 | | | | |
| | | JJR | Maitani, Y., et al., Influence of molecular weight and charge on nasal absorption of dextran and DEAE-dextran in rabbits, Int'l. J. Pharmaceut. 1989; 49: 23-27 | | | | |
| | | | McMartin, C., et al., Analysis of structural requirements for the absorption of drugs and macromolecules from the nasal cavity, J. Pharm. Sci. 1987; 76: 535-540 | | | | |



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|---|------|--|--|--|--|--|
| | XXR | Mori, I., et al., Temperature-sensitive parainfluenza type 1 vaccine virus directly accesses the central nervous system by infecting olfactory neurons. J. Gen. Virol. 1996; 77: 2121-4 | | | | |
| | LLR | Naumann, E., et al., Vasopressin and cognitive processes: two event-related potential studies. Peptides. 1991; 12: 1379-84 | | | | |
| | MMR | Pasechnik, V., et al., Macromolecular drug delivery to the CNS with protein carriers. Exp. Opin. Invest. Drugs 1996; 5:1255-1276 | | | | |
| | NNR | Paul, A., et al., Non-invasive Administration of Protein Antigens: Transdermal Immunization with Bovine Serum Albumine in Transfersomes. Vaccine Res. 1995; 4(3):145-164 | | | | |
| | OOR | Perras, B., et al., Sleep and signs of attention during 3 months of intranasal vasopressin: a pilot study in two elderly subjects. Peptides. 1996; 17: 1253-55 | | | | |
| | PPR | Pietrowsky, R., et al., Brain potential changes after intranasal vs. intravenous administration of vasopressin: Evidence for a direct nose- brain pathway for peptide effects in humans. Biol. Psychiatry. 1996; 39: 332-40 | | | | |
| | QQR | Pihoker, C., et al., Diagnostic studies with intravenous and intranasal growth hormone-releasing peptide-2 in children of short stature. J. Clin. Endocrinol. Metab. 1995; 80(10): 2987-92 | | | | |
| | RRR | Pohl, J., et al., Modulation of pain perception in man by a vasopressin analogue. Peptides. 1996; 17: 641-7 | | | | |
| | SSR | Sarkar, MA, Drug metabolism in the nasal mucosa. Pharm-Res. 1992; 9: 1-9 | | | | |
| | TTR | Shimoda, N., et al., Effects of dose, pH and osmolarity on intranasal absorption of recombinant human erythropoietin in rats, Biol. Pharm. Bull. 1995; 18(5): 734-9 | | | | |
| | UUR | Sperber, S.J., et al., Otologic effects of interferon beta serine in experimental rhinovirus colds, Arch. Otolaryngol. Head. Neck. Surg. 1992; 118: 933-6 | | | | |
| | VVR | Ting, T.Y., et al., Microparticles of polyvinyl alcohol for nasal delivery. I. Generation by spray-drying and spray-desolvation, Pharm. Res. 1992; 9: 1330-5 | | | | |
| | WWR | Tsume, Y, et al., Quantitative evaluation of the gastrointestinal absorption of protein into the blood and lymph circulation, Biol. Pharm. Bull. 1996; 19(10): 1332-1337 | | | | |
| | XXR | Watanabe, Y., et al., Absorption of recombinant human granulocyte colony-stimulating factor (rhG-CSF) and blood leukocyte dynamics following intranasal administration in rabbits, Biol. Pharm. Bull. 1993; 16: 93-5 | | | | |
| | YYR | Watanabe, Y., et al., Pharmacokinetics and pharmacodynamics of recombinant human granulocyte colony-stimulating factor (rhG-CSF) following intranasal administration in rabbits, J. Drug Target. 1995; 3: 231-38 | | | | |
| | ZZR | Wearley, L.L., Recent progress in protein and peptide delivery by noninvasive routes, Crit. Rev. Ther. Drug Carrier Syst. 1991; 8: 331-94 | | | | |
| | AAAR | Westenberg, H.G., et al., Pharmacokinetics of DGAVP in plasma following intranasal and oral administration to healthy subjects, Peptides, 1994; 15: 1101-4 | | | | |
| ↓ | BBBR | Van der Wiel, H.E., et al., Intranasal calcitonin suppresses increased bone resorption during short-term immobilization: A double-blind study of the effects of intranasal calcitonin on biochemical parameters of bone turnover. J. Bone Mineral Res. 1993; 8:1459-65 | | | | |

Examiner /Bruce Hissong/

Date Considered: 07/23/2006

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP § 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.